

### **REMARKS/ARGUMENTS**

Claims 1-96 were pending in this application. In the Office action dated December 11, 2007, claims 9-67 and 74-96 were withdrawn by the Office, due to a restriction requirement. Applicants acknowledge allowance of claims 68-73. With this response, claim 1 has been amended. Accordingly, claims 1-8 and 68-73 are currently pending in above-mentioned application. Applicants request reconsideration and rejoining of claims 9-67 and 74-96, in view of amendments to claim 1.

### **RESPONSE UNDER 37 C.F.R. 1.121**

In response to the Office Action dated May 5, 2008, Applicants provided the amended paragraph of the specification with markings and the status identifier to claim 96, both of which were inadvertently omitted by the Applicants. Applicants respectfully request that the Office enter Applicants' amendment and response pursuant to 37 C.F.R. §1.111.

### **EXAMINER INTERVIEW UNDER 37 C.F.R. 1.133**

Applicants thank Examiners Spieler and Keshor for granting an interview on March 19, 2008. Applicants discussed the Examiner's reconsideration of Applicants' initial election with traverse and issues with the restriction requirement being made final in the Office action dated December 11, 2007. Applicants discussed with the Examiners an amendment to claim 1 that provides a linking claim to claims 9-67 and 74-96. Applicants also addressed the rejections of record with the Examiners. Agreement was reached with the Examiners that Office would reconsider rejoining of claims 9-67 and 74-96, in view of amendments to claim 1.

### **ELECTION/RESTRICTION**

Claims 9-67 and 74-96 were withdrawn by the Office from further consideration pursuant to 37 C.F.R. §1.142(b), as being drawn to a non-elected Group and species, there being no allowable generic or linking claim. Applicants traverse the final restriction requirement in view of amendments to claim 1. In claim 1, Applicants claim a water-soluble drug-polymer conjugate selected from a Wortmannin-poly(ethylene glycol) conjugate of formula I, II, III, IV and V, that provides a linking claim to claims 9-67 and 74-96. Applicants

request reconsideration, withdrawal of the restriction requirement and rejoining of claims 9-67 and 74-96 (MPEP § 821.04).

#### **REJECTION UNDER 35 U.S.C. §112, 1<sup>st</sup> PARAGRAPH**

Claims 1-8 were rejected under 35 U.S.C. §112, 1<sup>st</sup> paragraph as failing to comply with the written description requirement. Applicants traverse the rejection in view of Applicants' amendments to claim 1. Applicants have further amended paragraph at page 3, lines 21-30 of the specification to remove the incorporation by reference of the publications cited therein. Applicants invention is clearly disclosed and claimed in the water-soluble Wortmannin-poly(ethylene glycol) conjugates defined in formulas I-V and complies in full with the written description requirement. Applicants' amendments to claim 1 and the paragraph at page 3, lines 21-30 of the specification obviate the Office's rejection of record. Applicants request that the Office withdraws the Section 112, first paragraph rejection of claims 1-8.

#### **REJECTION UNDER 35 U.S.C. §102**

Claims 1 and 2 were rejected by the Office under 35 U.S.C. §102(b), as being anticipated by a non-patent publication by L. Varticovski, et al. in the Journal of Controlled Release, Volume 74, Issue 1-3, July 6, 2001, pages 275-281 (Varticovski, et al.). Applicants respectfully disagree and traverse in view of amendments to claim 1.

Applicants claim in amended claim 1:

1. A water-soluble drug-polymer conjugate selected from a conjugate of formula I, II, III, IV and V:(emphasis added)

The Office relies on the Varticovski, et al. reference to disclose a water-soluble conjugate that includes a Wortmannin derivative 11-O-desacetylwortmannin (DAWN), a hydroxypropyl methacrylate (HPMA) copolymer and an oligopeptide (GFLG) to attach DAWN to HPMA. Applicants' claimed conjugates are Wortmannin-poly(ethylene glycol) conjugates. None of the conjugates disclosed in Varticovski, et al., suggest or teach Applicants' claimed conjugates, element for element, as required under 37 C.F. R. §1.104 and 35 U.S.C §102(b). Applicants respectfully submit that the Section 102(b) rejection is overcome and Applicants request the Office withdraw the rejection.

**REJECTION UNDER 35 U.S.C. §103**

Claims 3-8 were rejected by the Office under 35 U.S.C. §103(a), as being unpatentable over L. Varticovski, et al. in the Journal of Controlled Release, Volume 74, Issue 1-3, July 6, 2001, pages 275-281 (Varticovski, et al.) in view of M. E. Cardenas, et al. in the publication Trends in Biotechnology, Volume 16, Issue 10, October 1, 1998, pages 427-433 (Cardenas, et al.) and G. Razzini, et al. in The FASEB Journal, Volume 14, June 200, pages 1179-1187 (Razzini, et al.). Applicants traverse the rejection in view of amendments to claim 1.

The Office relies on the Varticovski, et al. reference to disclose a water-soluble conjugate that includes a Wortmannin derivative 11-O-desacetylwortmannin (DAWN), a hydroxypropyl methacrylate. The Office, however, concedes that the Varticovski, et al. reference does not teach the inhibition of mTOR-kinase, as claimed by Applicants. The Office relies on the Cardenas, et al. reference to disclose that Wortmannin is an inhibitor of PI 3-kinase and mTOR-kinase. The Cardenas, et al. reference does not suggest or disclose water-soluble Wortmannin-polymer conjugates or methods for using the conjugates as an inhibitor of PI 3-kinase and mTOR-kinase, as claimed by the Applicants. The Office further concedes that both the Varticovski, et al. reference and the Cardenas, et al. reference do not teach that PI 3-kinase inhibition is known to have therapeutic effects on several types of cancer. The Office relies on the Razzini, et al. reference to disclose potential cancer therapies based on PI 3-kinase antagonists inhibiting cell growth and tumorigenicity in human cancer cell lines. The Razzini, et al., however, reference does not suggest or disclose water-soluble Wortmannin-polymer conjugates or methods for using the conjugates as an inhibitor of PI 3-kinase or non-small cell lung cancer, as claimed by the Applicants. None of the references discloses or suggest Applicants claimed Wortmannin poly(ethylene glycol) conjugates or their claimed methods of inhibiting mTor-kinase, PI 3-kinase and or non-small cell lung cancer.

The references cited by the Office, whether taken individually or in combination as a whole, do not teach the Applicants invention. Applicants assert that the Office has not established a *prime facie* obviousness rejection under Section 103(a); MPEP 2143. The Office has improperly combined the three references, as there would be no motivation for one of ordinary skill in the art to combine the disclosure of the three references as a whole (see KSR Int'l. Col. v. Teleflex, Inc., No. 04-1350, U.S. April 30, 2007 and attached USPTO

memo from Margaret A. Focarino, May 3, 2007, "In formulating a rejection under Section 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed."). Applicants respectfully submit that the Section 103(a) rejection is overcome.

Claims 1-96 are in condition for immediate allowance and a notice to this effect is earnestly solicited.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Stephen E. Johnson', is written over a horizontal line.

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